

FIG. 1

Anatomy of an Intron

MAG GURAGU - - - - YNYURAY - - Y₁₂₋₁₅NC AG G

5' Splice Site
(Splice Donor)

Branch

3' Splice Site
(Splice Acceptor)

M = C or A

R = puRine (A or G)

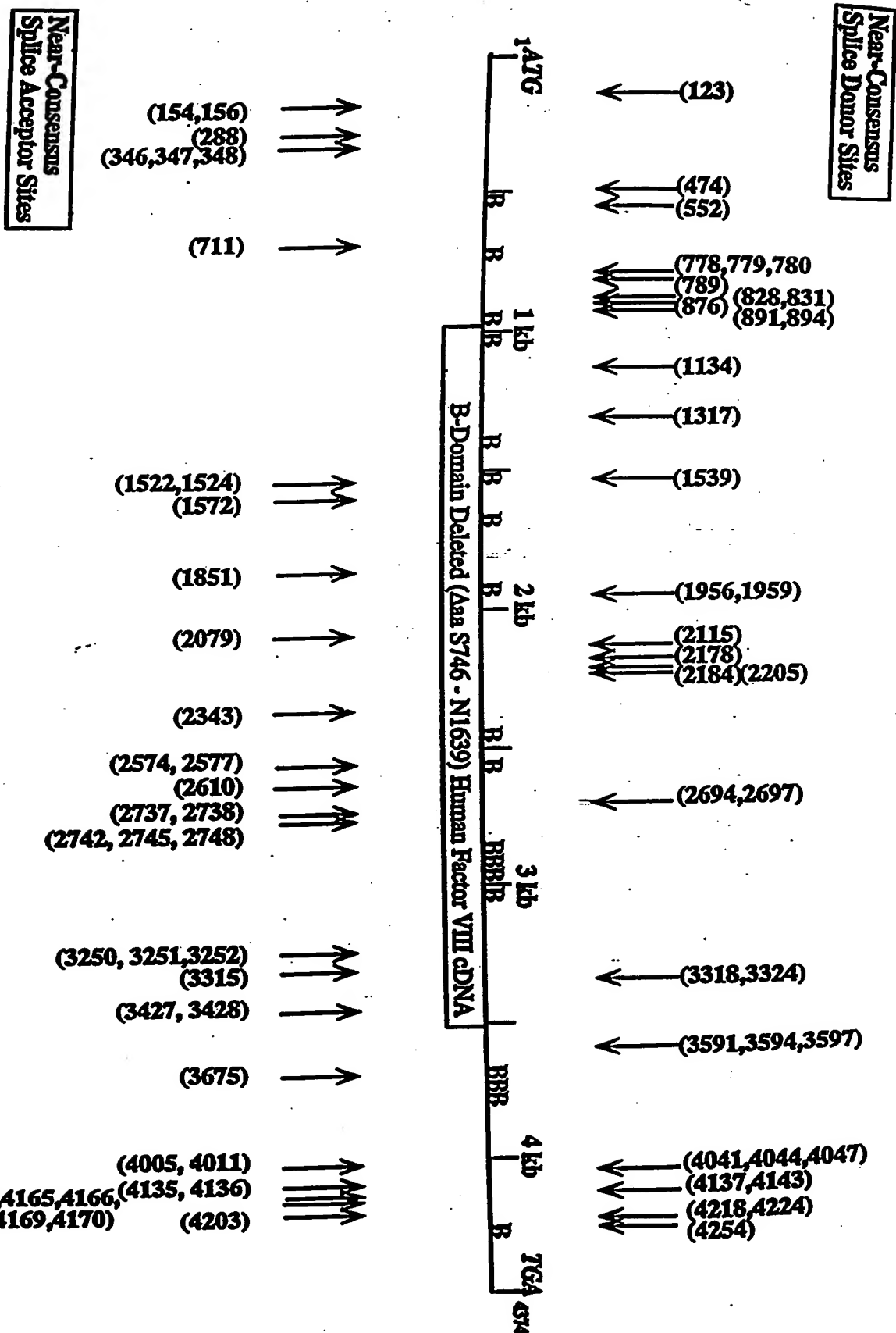
Y = pYrimidine (C or T or U)

Conservative Mutagenesis of Near Consensus 3' Splice sequence

TTC TCA GGA GAA
Phe Ser Gly Glu

Alternate Codons	
Ser	Gly
TCC	None
TCG	
TCT	

FIG. 3



B = Branch Sequence Sites

FIG. 4A

NC-Splice Donor Changes:

Location in Bayer BDD-Factor VIII cDNA	Nucleotide Change	Codon	Amino Acid
123	T → A	GGA	G
474	G A	CAA	Q
552	T C	GTT	V
778	T A	AGC	S
779	C G	AGC	S
780	T C	AGC	S
789	T A	GGA	G
828	G T	GTT	V
831	T A	ATA	I
876	T A	GGA	G
891	G T	GTT	V
894	G A	AGA	R
1134	G A	AGA	R
1317	T A	GGA	G
1539	T A	GGA	G
1956	G A	GAA	E
1959	G A	GTA	V
2115	G A	GGA	G
2178	G A	AAA	K
2184	T A	TCC	S
2205	T A	GGA	G
2694	A T	GTT	V
2697	T C	ACC	T
3318	T A	GGA	G
3324	T C	TTC	F
3591	G A	AAA	K
3594	G T	GTT	V
3597	G T	GAC	D
4041	G A	CAA	Q
4044	G T	GTT	V
4047	G T	AAC	N
4137	T C	TCT	S
4143	T C	TAC	Y
4218	G A	AAA	K
4224	T C	TTC	F
4254	G C	GTC	V

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FIG. 4B

NC-Splice Acceptor Changes

Location in Bayer BDD-Factor VIII cDNA	Nucleotide change	Codon	Amino Acid
154	A → C	CGC	R
156	A → C	CGC	R
288	G → A	CAA	Q
346	A → T	TCC	S
347	G → C	TCC	S
348	T → C	TCC	S
711	G → A	CAA	Q
1522	A → C	CGC	R
1524	G → C	CGC	R
1572	A → C	CCC	P
1851	A → C	CCC	P
2079	A → C	TCC	S
2343	G → A	CAA	Q
2574	T → A	GTA	V
2577	T → A	GTA	V
2610	G → A	CAA	Q
2737	A → T	TCC	S
2738	G → C	TCC	S
2742	T → C	CTC	L
2745	T → A	ATA	I
2748	T → A	TCA	S
3250	A → T	TCC	S
3251	G → C	TCC	S
3252	T → C	TCC	S
3315	A → C	CCC	P
3427	A → T	TCC	S
3428	G → C	TCC	S
3675	G → A	CAA	Q
4005	T → A	CTA	L
4011	T → A	CTA	L
4135	A → T	TCT	S
4136	G → C	TCC	S
4161	C → A	ATA	I
4164	C → G	TCG	S
4165	A → T	TCG	S
4166	G → C	TCG	S
4167	C → G	TCG	S
4168	A → T	TCG	S
4169	G → C	TCG	S
4170	T → G	TCG	S
4203	G → A	CAA	Q

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[illegible]

Location in Bayer BDD-Factor VIII cDNA

[illegible]

Position	Sequence	Sequence	Sequence
504	T	C	S
703	T	C	L
705	G	C	L
955	T	C	L
957	G	C	L
1110	T	C	T
1441	T	C	L
1443	G	C	L
1500	T	C	T
1668	T	C	V
1923	T	C	S
2406	T	C	S
2592	T	C	T
2892	T	C	S
2898	T	C	V
2955	T	C	T
3024	T	C	S
3696	T	C	L
3742	T	C	L
3744	A	C	L
3795	T	C	F
4281	G	C	L

[illegible]

530 535 540 545 550 555 560 565 570 575
 * * * * * * * * * *

FIG. 5C

pDJCcoding TAT CTT TCT CAT GTG GAC CTG GTT AAA GAC TTG AAT TCA GGC CTC ATT
 1. p25Dco530 540 550 560 570
 [16902] TAT CTT TCT CAT GTG GAC CTG GTT AAA GAC TTG AAT TCA GGC CTC ATT>
 pDJCcoding TAT CTT TCT CAT GTG GAC CTG GTT AAA GAC TTG AAT TCA GGC CTC ATT

580 585 590 595 600 605 610 615 620
 * * * * *
 pDJCcoding GGA GCC CTA CTA GTA TGT AGA GAA GGG AGT CTG GCC AAG GAA AAG ACA
 1. p25Dcod 580 590 600 610 620
 [16902] GGA GCC CTA CTA GTA TGT AGA GAA GGG AGT CTG GCC AAG GAA AAG ACA>
 pDJCcoding GGA GCC CTA CTA GTA TGT AGA GAA GGG AGT CTG GCC AAG GAA AAG ACA

625 630 635 640 645 650 655 660 665 670
 * * * * *
 pDJCcoding CAG ACC TTG CAC AAA TTT ATA CTA CTT TTT GCT GTA TTT GAT GAA GGG
 1. p25Dcod 630 640 650 660 670
 [16902] CAG ACC TTG CAC AAA TTT ATA CTA CTT TTT GCT GTA TTT GAT GAA GGG>
 pDJCcoding CAG ACC TTG CAC AAA TTT ATA CTA CTT TTT GCT GTA TTT GAT GAA GGG

675 680 685 690 695 700 705 710 715 720
 * * * * *
 pDJCcoding AAA AGT TGG CAC TCA GAA ACA AAG AAC TCC CTC ATG CAA GAT AGG GAT
 1. p25Dcod 680 690 700 710 720
 [16902] AAA AGT TGG CAC TCA GAA ACA AAG AAC TCC CTC ATG CAA GAT AGG GAT>
 pDJCcoding AAA AGT TGG CAC TCA GAA ACA AAG AAC TCC CTC ATG CAA GAT AGG GAT

725 730 735 740 745 750 755 760 765
 * * * * *
 pDJCcoding GCT GCA TCT GCT CGG GCC TGG CCT AAA ATG CAC ACA GTC AAT GGT TAT
 1. p25Dcod 730 740 750 760
 [16902] GCT GCA TCT GCT CGG GCC TGG CCT AAA ATG CAC ACA GTC AAT GGT TAT>
 pDJCcoding GCT GCA TCT GCT CGG GCC TGG CCT AAA ATG CAC ACA GTC AAT GGT TAT

770 775 780 785 790 795 800 805 810 815
 * * * * *
 pDJCcoding GTA AAC AGG AGC CTG CCA GGA CTG ATT GGA TGC CAC AGG AAA TCA GTC
 1. p25Dco770 780 790 800 810
 [16902] GTA AAC AGG tct CTG CCA GGT CTG ATT GGA TGC CAC AGG AAA TCA GTC>
 pDJCcoding GTA AAC AGG AGC CTG CCA GGA CTG ATT GGA TGC CAC AGG AAA TCA GTC

820 825 830 835 840 845 850 855 860
 * * * * *
 pDJCcoding TAT TGG CAT GTT ATA GGA ATG GGC ACC ACT CCT GAA GTG CAC TCA ATA

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[illegible][illegible]

FIG. 5E

^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^
 pDJCcoding CTT ACC GAT TCT GAA ATG GAT GTG GTC AGA TTT GAT GAT GAC AAC TCT

	1155	1160	1165	1170	1175	1180	1185	1190	1195	1200						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	CCT	TCC	TTT	ATC	CAA	ATT	CGC	TCA	GTT	GCC	AAG	AAG	CAT	CCT	AAA	ACT
1. p25Dcod		1160		1170		1180		1190		1200						
[16902]	CCT	TCC	TTT	ATC	CAA	ATT	CGC	TCA	GTT	GCC	AAG	AAG	CAT	CCT	AAA	ACT>
	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^
pDJCcoding	CCT	TCC	TTT	ATC	CAA	ATT	CGC	TCA	GTT	GCC	AAG	AAG	CAT	CCT	AAA	ACT

	1205	1210	1215	1220	1225	1230	1235	1240	1245							
	*	*	*	*	*	*	*	*	*							
pDJCcoding	TGG	GTA	CAT	TAC	ATT	GCT	GCT	GAA	GAG	GAG	GAC	TGG	GAC	TAT	GCT	CCC
1. p25Dcod		1210		1220		1230		1240								
[16902]	TGG	GTA	CAT	TAC	ATT	GCT	GCT	GAA	GAG	GAG	GAC	TGG	GAC	TAT	GCT	CCC>
	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^
pDJCcoding	TGG	GTA	CAT	TAC	ATT	GCT	GCT	GAA	GAG	GAG	GAC	TGG	GAC	TAT	GCT	CCC

	1250	1255	1260	1265	1270	1275	1280	1285	1290	1295						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	TTA	GTC	CTC	GCC	CCC	GAT	GAC	AGA	AGT	TAT	AAA	AGT	CAA	TAT	TTG	AAC
1. p25Dc1250		1260		1270		1280		1290								
[16902]	TTA	GTC	CTC	GCC	CCC	GAT	GAC	AGA	AGT	TAT	AAA	AGT	CAA	TAT	TTG	AAC>
	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^
pDJCcoding	TTA	GTC	CTC	GCC	CCC	GAT	GAC	AGA	AGT	TAT	AAA	AGT	CAA	TAT	TTG	AAC

	1300	1305	1310	1315	1320	1325	1330	1335	1340							
	*	*	*	*	*	*	*	*	*							
pDJCcoding	AAT	GGC	CCT	CAG	CGG	ATT	GGA	AGG	AAG	TAC	AAA	AAA	GTC	CGA	TTT	ATG
1. p25Dcod	1300		1310		1320		1330		1340							
[16902]	AAT	GGC	CCT	CAG	CGG	ATT	GGA	AGG	AAG	TAC	AAA	AAA	GTC	CGA	TTT	ATG>
	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^
pDJCcoding	AAT	GGC	CCT	CAG	CGG	ATT	GGA	AGG	AAG	TAC	AAA	AAA	GTC	CGA	TTT	ATG

	1345	1350	1355	1360	1365	1370	1375	1380	1385	1390						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	GCA	TAC	ACA	GAT	GAA	ACC	TTT	AAG	ACT	CGT	GAA	GCT	ATT	CAG	CAT	GAA
1. p25Dcod	1350		1360		1370		1380		1390							
[16902]	GCA	TAC	ACA	GAT	GAA	ACC	TTT	AAG	ACT	CGT	GAA	GCT	ATT	CAG	CAT	GAA>
	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^
pDJCcoding	GCA	TAC	ACA	GAT	GAA	ACC	TTT	AAG	ACT	CGT	GAA	GCT	ATT	CAG	CAT	GAA

	1395	1400	1405	1410	1415	1420	1425	1430	1435	1440						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	TCA	GGA	ATC	TTG	GGA	CCT	TTA	CTT	TAT	GGG	GAA	GTT	GGA	GAC	ACA	CTG
1. p25Dcod	1400		1410		1420		1430		1440							
[16902]	TCA	GGA	ATC	TTG	GGA	CCT	TTA	CTT	TAT	GGG	GAA	GTT	GGA	GAC	ACA	CTG>
	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^
pDJCcoding	TCA	GGA	ATC	TTG	GGA	CCT	TTA	CTT	TAT	GGG	GAA	GTT	GGA	GAC	ACA	CTG

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FIG. 5F

	1445	1450	1455	1460	1465	1470	1475	1480	1485							
	*	*	*	*	*	*	*	*	*							
pDJCcoding	CTC	ATT	ATA	TTT	AAG	AAT	CAA	GCA	AGC	AGA	CCA	TAT	AAC	ATC	TAC	CCT
1. p25Dcod		1450		1460		1470		1480								
(16902]	tTg	ATT	ATA	TTT	AAG	AAT	CAA	GCA	AGC	AGA	CCA	TAT	AAC	ATC	TAC	CCT>
	v^v	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^
pDJCcoding	CTC	ATT	ATA	TTT	AAG	AAT	CAA	GCA	AGC	AGA	CCA	TAT	AAC	ATC	TAC	CCT

	1490	1495	1500	1505	1510	1515	1520	1525	1530	1535						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	CAC	GGA	ATC	ACC	GAT	GTC	CGT	CCT	TTG	TAT	TCA	CGC	AGA	TTA	CCA	AAA
1. p25Dcod	1490		1500		1510		1520		1530							
(16902]	CAC	GGA	ATC	ACC	GAT	GTC	CGT	CCT	TTG	TAT	TCA	aGg	AGA	TTA	CCA	AAA>
	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^
pDJCcoding	CAC	GGA	ATC	ACC	GAT	GTC	CGT	CCT	TTG	TAT	TCA	CGC	AGA	TTA	CCA	AAA

	1540	1545	1550	1555	1560	1565	1570	1575	1580							
	*	*	*	*	*	*	*	*	*							
pDJCcoding	GGA	GTA	AAA	CAT	TTG	AAG	GAT	TTT	CCA	ATT	CTG	CCC	GGA	GAA	ATA	TTC
1. p25Dcod	1540		1550		1560		1570		1580							
(16902]	GGt	GTA	AAA	CAT	TTG	AAG	GAT	TTT	CCA	ATT	CTG	CCa	GGA	GAA	ATA	TTC>
	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^
pDJCcoding	GGA	GTA	AAA	CAT	TTG	AAG	GAT	TTT	CCA	ATT	CTG	CCC	GGA	GAA	ATA	TTC

	1585	1590	1595	1600	1605	1610	1615	1620	1625	1630						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	AAA	TAT	AAA	TGG	ACA	GTG	ACT	GTA	GAA	GAT	GGG	CCA	ACT	AAA	TCA	GAT
1. p25Dcod	1590		1600		1610		1620		1630							
(16902]	AAA	TAT	AAA	TGG	ACA	GTG	ACT	GTA	GAA	GAT	GGG	CCA	ACT	AAA	TCA	GAT>
	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^
pDJCcoding	AAA	TAT	AAA	TGG	ACA	GTG	ACT	GTA	GAA	GAT	GGG	CCA	ACT	AAA	TCA	GAT

	1635	1640	1645	1650	1655	1660	1665	1670	1675	1680						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	CCT	CGG	TGC	CTG	ACC	CGC	TAT	TAC	TCT	AGT	TTC	GTC	AAT	ATG	GAG	AGA
1. p25Dcod	1640		1650		1660		1670		1680							
(16902]	CCT	CGG	TGC	CTG	ACC	CGC	TAT	TAC	TCT	AGT	TTC	GTC	AAT	ATG	GAG	AGA>
	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^
pDJCcoding	CCT	CGG	TGC	CTG	ACC	CGC	TAT	TAC	TCT	AGT	TTC	GTC	AAT	ATG	GAG	AGA

	1685	1690	1695	1700	1705	1710	1715	1720	1725							
	*	*	*	*	*	*	*	*	*							
pDJCcoding	GAT	CTA	GCT	TCA	GGA	CTC	ATT	GGC	CCT	CTC	CTC	ATC	TGC	TAC	AAA	GAA
1. p25Dcod	1690		1700		1710		1720									
(16902]	GAT	CTA	GCT	TCA	GGA	CTC	ATT	GGC	CCT	CTC	CTC	ATC	TGC	TAC	AAA	GAA>
	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^	^v^
pDJCcoding	GAT	CTA	GCT	TCA	GGA	CTC	ATT	GGC	CCT	CTC	CTC	ATC	TGC	TAC	AAA	GAA

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FIG. 56

	1730	1735	1740	1745	1750	1755	1760	1765	1770	1775						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	TCT	GTA	GAT	CAA	AGA	GGA	AAC	CAG	ATA	ATG	TCA	GAC	AAG	AGG	AAT	GTC
1. p25Dc1730			1740			1750		1760		1770						
(16902)	TCT	GTA	GAT	CAA	AGA	GGA	AAC	CAG	ATA	ATG	TCA	GAC	AAG	AGG	AAT	GTC>
	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^
pDJCcoding	TCT	GTA	GAT	CAA	AGA	GGA	AAC	CAG	ATA	ATG	TCA	GAC	AAG	AGG	AAT	GTC

	1780	1785	1790	1795	1800	1805	1810	1815	1820							
	*	*	*	*	*	*	*	*	*							
pDJCcoding	ATC	CTG	TTT	TCT	GTA	TTT	GAT	GAG	AAC	CGA	AGC	TGG	TAC	CTC	ACA	GAG
1. p25Dcod 1780			1790		1800		1810		1820							
(16902)	ATC	CTG	TTT	TCT	GTA	TTT	GAT	GAG	AAC	CGA	AGC	TGG	TAC	CTC	ACA	GAG>
	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^
pDJCcoding	ATC	CTG	TTT	TCT	GTA	TTT	GAT	GAG	AAC	CGA	AGC	TGG	TAC	CTC	ACA	GAG

	1825	1830	1835	1840	1845	1850	1855	1860	1865	1870						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	AAT	ATA	CAA	CGC	TTT	CTC	CCC	AAT	CCC	GCT	GGA	GTG	CAG	CTT	GAG	GAT
1. p25Dcod 1830			1840		1850		1860		1870							
(16902)	AAT	ATA	CAA	CGC	TTT	CTC	CCC	AAT	CCC	GCT	GGA	GTG	CAG	CTT	GAG	GAT>
	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^
pDJCcoding	AAT	ATA	CAA	CGC	TTT	CTC	CCC	AAT	CCC	GCT	GGA	GTG	CAG	CTT	GAG	GAT

	1875	1880	1885	1890	1895	1900	1905	1910	1915	1920						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	CCA	GAG	TTC	CAA	GCC	TCC	AAC	ATC	ATG	CAC	AGC	ATC	AAT	GGC	TAT	GTT
1. p25Dcod 1880			1890		1900		1910		1920							
(16902)	CCA	GAG	TTC	CAA	GCC	TCC	AAC	ATC	ATG	CAC	AGC	ATC	AAT	GGC	TAT	GTT>
	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^
pDJCcoding	CCA	GAG	TTC	CAA	GCC	TCC	AAC	ATC	ATG	CAC	AGC	ATC	AAT	GGC	TAT	GTT

	1925	1930	1935	1940	1945	1950	1955	1960	1965							
	*	*	*	*	*	*	*	*	*							
pDJCcoding	TTC	GAT	AGT	TTG	CAG	TTG	TCA	GTT	TGT	TTG	CAT	GAA	GTA	GCA	TAC	TGG
1. p25Dcod 1930			1940		1950		1960									
(16902)	TTC	GAT	AGT	TTG	CAG	TTG	TCA	GTT	TGT	TTG	CAT	GAG	GTG	GCA	TAC	TGG>
	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^
pDJCcoding	TTC	GAT	AGT	TTG	CAG	TTG	TCA	GTT	TGT	TTG	CAT	GAA	GTA	GCA	TAC	TGG

	1970	1975	1980	1985	1990	1995	2000	2005	2010	2015						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	TAC	ATT	CTA	AGC	ATT	GGA	GCA	CAG	ACT	GAC	TTC	CTT	TCT	GTC	TTC	TTC
1. p25Dc1970			1980		1990		2000		2010							
(16902)	TAC	ATT	CTA	AGC	ATT	GGA	GCA	CAG	ACT	GAC	TTC	CTT	TCT	GTC	TTC	TTC>
	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^
pDJCcoding	TAC	ATT	CTA	AGC	ATT	GGA	GCA	CAG	ACT	GAC	TTC	CTT	TCT	GTC	TTC	TTC

2020	2025	2030	2035	2040	2045	2050	2055	2060
*	*	*	*	*	*	*	*	*

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	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	2101	2102	2103	2104	2105	2106	2107	2108	2109	2110	2111	2112	2113	2114	2115	2116	2117	2118	2119	2120	2121	2122	2123	2124	2125	2126	2127	2128	2129	2130	2131	2132	2133	2134	2135	2136	2137	2138	2139	2140	2141	2142	2143	2144	2145	2146	2147	2148	2149	2150	2151	2152	2153	2154	2155	2156	2157	2158	2159	2160	2161	2162	2163	2164	2165	2166	2167	2168	2169	2170	2171	2172	2173	2174	2175	2176	2177	2178	2179	2180	2181	2182	2183	2184	2185	2186	2187	2188	2189	2190	2191	2192	2193	2194	2195	2196	2197	2198	2199	2200	2201	2202	2203	2204	2205	2206	2207	2208	2209	2210	2211	2212	2213	2214	2215	2216	2217	2218	2219	2220	2221	2222	2223	2224	2225	2226	2227	2228	2229	2230	2231	2232	2233	2234	2235	2236	2237	2238	2239	2240	2241	2242	2243	2244	2245	2246	2247	2248	2249	2250	2251	2252	2253	2254	2255	2256	2257	2258	2259	2260	2261	2262	2263	2264	2265	2266	2267	2268	2269	2270	2271	2272	2273	2274	2275	2276	2277	2278	2279	2280	2281	2282	2283	2284	2285	2286	2287	2288	2289	2290	2291	2292	2293	2294	2295	2296	2297	2298	2299	2300	2301	2302	2303	2304	2305	2306	2307	2308	2309	2310	2311	2312	2313	2314	2315	2316	2317	2318	2319	2320	2321	2322	2323	2324	2325	2326	2327	2328	2329	2330	2331	2332	2333	2334	2335	2336	2337	2338	2339	2340	2341	2342	2343	2344	2345	2346	2347	2348	2349	2350	2351	2352	2353	2354	2355	2356	2357	2358	2359	2360	2361	2362	2363	2364	2365	2366	2367	2368	2369	2370	2371	2372	2373	2374	2375	2376	2377	2378	2379	2380	2381	2382	2383	2384	2385	2386	2387	2388	2389	2390	2391	2392	2393	2394	2395	2396	2397	2398	2399	2400	2401	2402	2403	2404	2405	2406	2407	2408	2409	2410	2411	2412	2413	2414	2415	2416	2417	2418	2419	2420	2421	2422	2
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2595 2600 2605 2610 2615 2620 2625 2630 2635 2640
 * * * * * * * *
 pDJccoding GAT GGC TCC TTT ACT CAA CCC TTA TAC CGT GGA GAA CTA AAT GAA CAT
 | | | |
 1. p25Dcod 2600 2610 2620 2630 2640
 [16902] GAT GGC TCC TTT ACT CAG CCC TTA TAC CGT GGA GAA CTA AAT GAA CAT>

FIG. 5J

^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^
 pDJCcoding GAT GGC TCC TTT ACT CAA CCC TTA TAC CGT GGA GAA CTA AAT GAA CAT

2645 2650 2655 2660 2665 2670 2675 2680 2685
 * * * * *
 pDJCcoding TTG GGA CTC CTG GGG CCA TAT ATA AGA GCA GAA GTT GAA GAT AAT ATC

1. p25Dcod 2650 2660 2670 2680
 [16902] TTG GGA CTC CTG GGG CCA TAT ATA AGA GCA GAA GTT GAA GAT AAT ATC>
 ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^
 pDJCcoding TTG GGA CTC CTG GGG CCA TAT ATA AGA GCA GAA GTT GAA GAT AAT ATC

2690 2695 2700 2705 2710 2715 2720 2725 2730 2735
 * * * * *
 pDJCcoding ATG GTT ACC TTC AGA AAT CAG GCC TCT CGT CCC TAT TCC TTC TAT TCT

1. p25Dcod 2690 2700 2710 2720 2730
 [16902] ATG GTT ACC TTC AGA AAT CAG GCC TCT CGT CCC TAT TCC TTC TAT TCT>
 ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^
 pDJCcoding ATG GTT ACC TTC AGA AAT CAG GCC TCT CGT CCC TAT TCC TTC TAT TCT

2740 2745 2750 2755 2760 2765 2770 2775 2780
 * * * * *
 pDJCcoding TCC CTC ATA TCA TAT GAG GAA GAT CAG AGG CAA GGA GCA GAA CCT AGA

1. p25Dcod 2740 2750 2760 2770 2780
 [16902] agC CTt ATT Tct TAT GAG GAA GAT CAG AGG CAA GGA GCA GAA CCT AGA>
 ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^
 pDJCcoding TCC CTC ATA TCA TAT GAG GAA GAT CAG AGG CAA GGA GCA GAA CCT AGA

2785 2790 2795 2800 2805 2810 2815 2820 2825 2830
 * * * * *
 pDJCcoding AAA AAC TTT GTC AAG CCT AAT GAA ACC AAA ACT TAC TTT TGG AAA GTG

1. p25Dcod 2790 2800 2810 2820 2830
 [16902] AAA AAC TTT GTC AAG CCT AAT GAA ACC AAA ACT TAC TTT TGG AAA GTG>
 ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^
 pDJCcoding AAA AAC TTT GTC AAG CCT AAT GAA ACC AAA ACT TAC TTT TGG AAA GTG

2835 2840 2845 2850 2855 2860 2865 2870 2875 2880
 * * * * *
 pDJCcoding CAA CAT CAT ATG GCA CCC ACT AAA GAT GAG TTT GAC TGC AAA GCC TGG

1. p25Dcod 2840 2850 2860 2870 2880
 [16902] CAA CAT CAT ATG GCA CCC ACT AAA GAT GAG TTT GAC TGC AAA GCC TGG>
 ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^
 pDJCcoding CAA CAT CAT ATG GCA CCC ACT AAA GAT GAG TTT GAC TGC AAA GCC TGG

2885 2890 2895 2900 2905 2910 2915 2920 2925
 * * * * *
 pDJCcoding GCT TAT TTC TCC GAT GTC GAC CTG GAA AAA GAT GTG CAC TCA GGC CTG

1. p25Dcod 2890 2900 2910 2920
 [16902] GCT TAT TTC Tct GAT GTt GAC CTG GAA AAA GAT GTG CAC TCA GGC CTG>
 ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^ ^^^
 pDJCcoding GCT TAT TTC TCC GAT GTC GAC CTG GAA AAA GAT GTG CAC TCA GGC CTG

000210-0922500

	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	2101	2102	2103	2104	2105	2106	2107	2108	2109	2110	2111	2112	2113	2114	2115	2116	2117	2118	2119	2120	2121	2122	2123	2124	2125	2126	2127	2128	2129	2130	2131	2132	2133	2134	2135	2136	2137	2138	2139	2140	2141	2142	2143	2144	2145	2146	2147	2148	2149	2150	2151	2152	2153	2154	2155	2156	2157	2158	2159	2160	2161	2162	2163	2164	2165	2166	2167	2168	2169	2170	2171	2172	2173	2174	2175	2176	2177	2178	2179	2180	2181	2182	2183	2184	2185	2186	2187	2188	2189	2190	2191	2192	2193	2194	2195	2196	2197	2198	2199	2200	2201	2202	2203	2204	2205	2206	2207	2208	2209	2210	2211	2212	2213	2214	2215	2216	2217	2218	2219	2220	2221	2222	2223	2224	2225	2226	2227	2228	2229	2230	2231	2232	2233	2234	2235	2236	2237	2238	2239	2240	2241	2242	2243	2244	2245	2246	2247	2248	2249	2250	2251	2252	2253	2254	2255	2256	2257	2258	2259	2260	2261	2262	2263	2264	2265	2266	2267	2268	2269	2270	2271	2272	2273	2274	2275	2276	2277	2278	2279	2280	2281	2282	2283	2284	2285	2286	2287	2288	2289	2290	2291	2292	2293	2294	2295	2296	2297	2298	2299	2300	2301	2302	2303	2304	2305	2306	2307	2308	2309	2310	2311	2312	2313	2314	2315	2316	2317	2318	2319	2320	2321	2322	2323	2324	2325	2326	2327	2328	2329	2330	2331	2332	2333	2334	2335	2336	2337	2338	2339	2340	2341	2342	2343	2344	2345	2346	2347	2348	2349	2350	2351	2352	2353	2354	2355	2356	2357	2358	2359	2360	2361	2362	2363	2364	2365	2366	2367	2368	2369	2370	2371	2372	2373	2374	2375	2376	2377	2378	2379	2380	2381	2382	2383	2384	2385	2386	2387	2388	2389	2390	2391	2392	2393	2394	2395	2396	2397	2398	2399	2400	2401	2402	2403	2404	2405	2406	2407	2408	2409	2410	2411	2412	2413	2414	2415	2416	2417	2418	2419	2420	2421	2422	2
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	3170	3175	3180	3185	3190	3195	3200	3205	3210	3215						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	TTA	GTA	ATG	GCT	CAG	GAT	CAA	AGG	ATT	CGA	TGG	TAT	CTG	CTC	AGC	ATG
1. p25Dc3170			3180		3190		3200		3210							
(16902)	TTA	GTA	ATG	GCT	CAG	GAT	CAA	AGG	ATT	CGA	TGG	TAT	CTG	CTC	AGC	ATG>
	AAA	AAA	AAA	AAA	AAA	AAA	AAA	AAA	AAA	AAA	AAA	AAA	AAA	AAA	AAA	AAA
pDJCcoding	TTA	GTA	ATG	GCT	CAG	GAT	CAA	AGG	ATT	CGA	TGG	TAT	CTG	CTC	AGC	ATG

[illegible]

3505 3510 3515 3520 3525 3530 3535 3540 3545 3550

FIG. 5M

pDJCcoding GGA CAG TGG GGC CCA AAG CTG GCC AGA CTT CAT TAT TCC GGA TCA ATC
 1. p25Dcod 3510 3520 3530 3540 3550
 [16902] GGA CAG TGG GGC CCA AAG CTG GCC AGA CTT CAT TAT TCC GGA TCA ATC>
 pDJCcoding GGA CAG TGG GGC CCA AAG CTG GCC AGA CTT CAT TAT TCC GGA TCA ATC
 3555 3560 3565 3570 3575 3580 3585 3590 3595 3600
 pDJCcoding AAT GCC TGG AGC ACC AAG GAG CCC TTT TCT TGG ATC AAA GTT GAC CTG
 1. p25Dcod 3560 3570 3580 3590 3600
 [16902] AAT GCC TGG AGC ACC AAG GAG CCC TTT TCT TGG ATC AAG GTT GAT CTG>
 pDJCcoding AAT GCC TGG AGC ACC AAG GAG CCC TTT TCT TGG ATC AAA GTT GAC CTG
 3605 3610 3615 3620 3625 3630 3635 3640 3645
 pDJCcoding TTG GCA CCA ATG ATT ATT CAC GGC ATC AAG ACC CAG GGT GCC CGT CAG
 1. p25Dcod 3610 3620 3630 3640
 [16902] TTG GCA CCA ATG ATT ATT CAC GGC ATC AAG ACC CAG GGT GCC CGT CAG>
 pDJCcoding TTG GCA CCA ATG ATT ATT CAC GGC ATC AAG ACC CAG GGT GCC CGT CAG
 3650 3655 3660 3665 3670 3675 3680 3685 3690 3695
 pDJCcoding AAG TTC TCC AGC CTC TAC ATC TCT CAA TTT ATC ATC ATG TAT AGT CTC
 1. p25Dcod 3650 3660 3670 3680 3690
 [16902] AAG TTC TCC AGC CTC TAC ATC TCT CAA TTT ATC ATC ATG TAT AGT CTC>
 pDJCcoding AAG TTC TCC AGC CTC TAC ATC TCT CAA TTT ATC ATC ATG TAT AGT CTC
 3700 3705 3710 3715 3720 3725 3730 3735 3740
 pDJCcoding GAT GGG AAG AAG TGG CAG ACT TAT CGA GGA AAT TCC ACT GGA ACC CTC
 1. p25Dcod 3700 3710 3720 3730 3740
 [16902] GAT GGG AAG AAG TGG CAG ACT TAT CGA GGA AAT TCC ACT GGA ACC CTC>
 pDJCcoding GAT GGG AAG AAG TGG CAG ACT TAT CGA GGA AAT TCC ACT GGA ACC CTC
 3745 3750 3755 3760 3765 3770 3775 3780 3785 3790
 pDJCcoding ATG GTC TTC TTT GGC AAT GTG GAT TCA TCT GGG ATA AAA CAC AAT ATT
 1. p25Dcod 3750 3760 3770 3780 3790
 [16902] ATG GTC TTC TTT GGC AAT GTG GAT TCA TCT GGG ATA AAA CAC AAT ATT>
 pDJCcoding ATG GTC TTC TTT GGC AAT GTG GAT TCA TCT GGG ATA AAA CAC AAT ATT
 3795 3800 3805 3810 3815 3820 3825 3830 3835 3840
 pDJCcoding TTC AAC CCT CCA ATT ATT GCT CGA TAC ATC CGT TTG CAC CCA ACT CAT

000210-09225500

FIG. 5N

1. p25Dcod 3800 3810 3820 3830 3840
 (16902] TTT AAC OCT CCA ATT ATT GCT CGA TAC ATC CGT TTG CAC CCA ACT CAT>
 pDJCcoding TTC AAC OCT CCA ATT ATT GCT CGA TAC ATC CGT TTG CAC CCA ACT CAT

3845 3850 3855 3860 3865 3870 3875 3880 3885
 * * * * *
 pDJCcoding TAT AGC ATT CGC AGC ACT CTT CGC ATG GAG TTG ATG GGC TGT GAT TTA
 | | | | |
 1. p25Dcod 3850 3860 3870 3880
 (16902] TAT AGC ATT CGC AGC ACT CTT CGC ATG GAG TTG ATG GGC TGT GAT TTA>
 | | | | |
 pDJCcoding TAT AGC ATT CGC AGC ACT CTT CGC ATG GAG TTG ATG GGC TGT GAT TTA

3890 3895 3900 3905 3910 3915 3920 3925 3930 3935
 * * * * *
 pDJCcoding AAT AGT TGC AGC ATG CCA TTG GGA ATG GAG AGT AAA GCA ATA TCA GAT
 | | | | |
 1. p25Dc3890 3900 3910 3920 3930
 (16902] AAT AGT TGC AGC ATG CCA TTG GGA ATG GAG AGT AAA GCA ATA TCA GAT>
 | | | | |
 pDJCcoding AAT AGT TGC AGC ATG CCA TTG GGA ATG GAG AGT AAA GCA ATA TCA GAT

3940 3945 3950 3955 3960 3965 3970 3975 3980
 * * * * *
 pDJCcoding GCA CAG ATT ACT GCT TCA TCC TAC TTT ACC AAT ATG TTT GCC ACC TGG
 | | | | |
 1. p25Dcod 3940 3950 3960 3970 3980
 (16902] GCA CAG ATT ACT GCT TCA TCC TAC TTT ACC AAT ATG TTT GCC ACC TGG>
 | | | | |
 pDJCcoding GCA CAG ATT ACT GCT TCA TCC TAC TTT ACC AAT ATG TTT GCC ACC TGG

3985 3990 3995 4000 4005 4010 4015 4020 4025 4030
 * * * * *
 pDJCcoding TCT OCT TCA AAA GCT CGA CTA CAC CTA CAA GGG AGG AGT AAT GCC TGG
 | | | | |
 1. p25Dcod 3990 4000 4010 4020 4030
 (16902] TCT OCT TCA AAA GCT CGA CTA CAC CTA CAA GGG AGG AGT AAT GCC TGG>
 | | | | |
 pDJCcoding TCT OCT TCA AAA GCT CGA CTA CAC CTA CAA GGG AGG AGT AAT GCC TGG

4035 4040 4045 4050 4055 4060 4065 4070 4075 4080
 * * * * *
 pDJCcoding AGA OCT CAA GTT AAC AAT CCA AAA GAG TGG CTG CAA GTG GAC TTC CAG
 | | | | |
 1. p25Dcod 4040 4050 4060 4070 4080
 (16902] AGA OCT CAG GTT AAT AAT CCA AAA GAG TGG CTG CAA GTG GAC TTC CAG>
 | | | | |
 pDJCcoding AGA OCT CAA GTT AAC AAT CCA AAA GAG TGG CTG CAA GTG GAC TTC CAG

4085 4090 4095 4100 4105 4110 4115 4120 4125
 * * * * *
 pDJCcoding AAG ACA ATG AAA GTC ACA GGA GTA ACT ACT CAG GGA GTA AAA TCT CTG
 | | | | |
 1. p25Dcod 4090 4100 4110 4120
 (16902] AAG ACA ATG AAA GTC ACA GGA GTA ACT ACT CAG GGA GTA AAA TCT CTG>

000270-89225600

[illegible]

	4130	4135	4140	4145	4150	4155	4160	4165	4170	4175						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	CTT	ACC	TCT	ATG	TAC	GTG	AAG	GAG	TTC	CTC	ATA	TCG	TCG	TCG	CAA	GAT
1. p25Dc	4130			4140			4150			4160				4170		
[16902]	CTT	ACC	agc	ATG	TAt	GTG	AAG	GAG	TTC	CTC	ATc	TCc	agc	agt	CAA	GAT>
	^^^	^^^	vvv	^^^	^^v	^^^	^^^	^^^	^^^	^^^	^^v	^^v	vvv	vvv	^^^	^^^
pDJCcoding	CTT	ACC	TCT	ATG	TAC	GTG	AAG	GAG	TTC	CTC	ATA	TCG	TCG	TCG	CAA	GAT

	4180	4185	4190	4195	4200	4205	4210	4215	4220							
	*	*	*	*	*	*	*	*	*							
pDJCcoding	GGC	CAT	CAG	TGG	ACT	CTC	TTT	TTT	CAA	AAT	GGC	AAA	GTA	AAA	GTT	TTC
1. p25Dcod	4180			4190			4200		4210			4220				
[16902]	GGC	CAT	CAG	TGG	ACT	CTC	TTT	TTT	CAG	AAT	GGC	AAA	GTA	AAG	GTT	TTT>
	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^
pDJCcoding	GGC	CAT	CAG	TGG	ACT	CTC	TTT	TTT	CAA	AAT	GGC	AAA	GTA	AAA	GTT	TTC

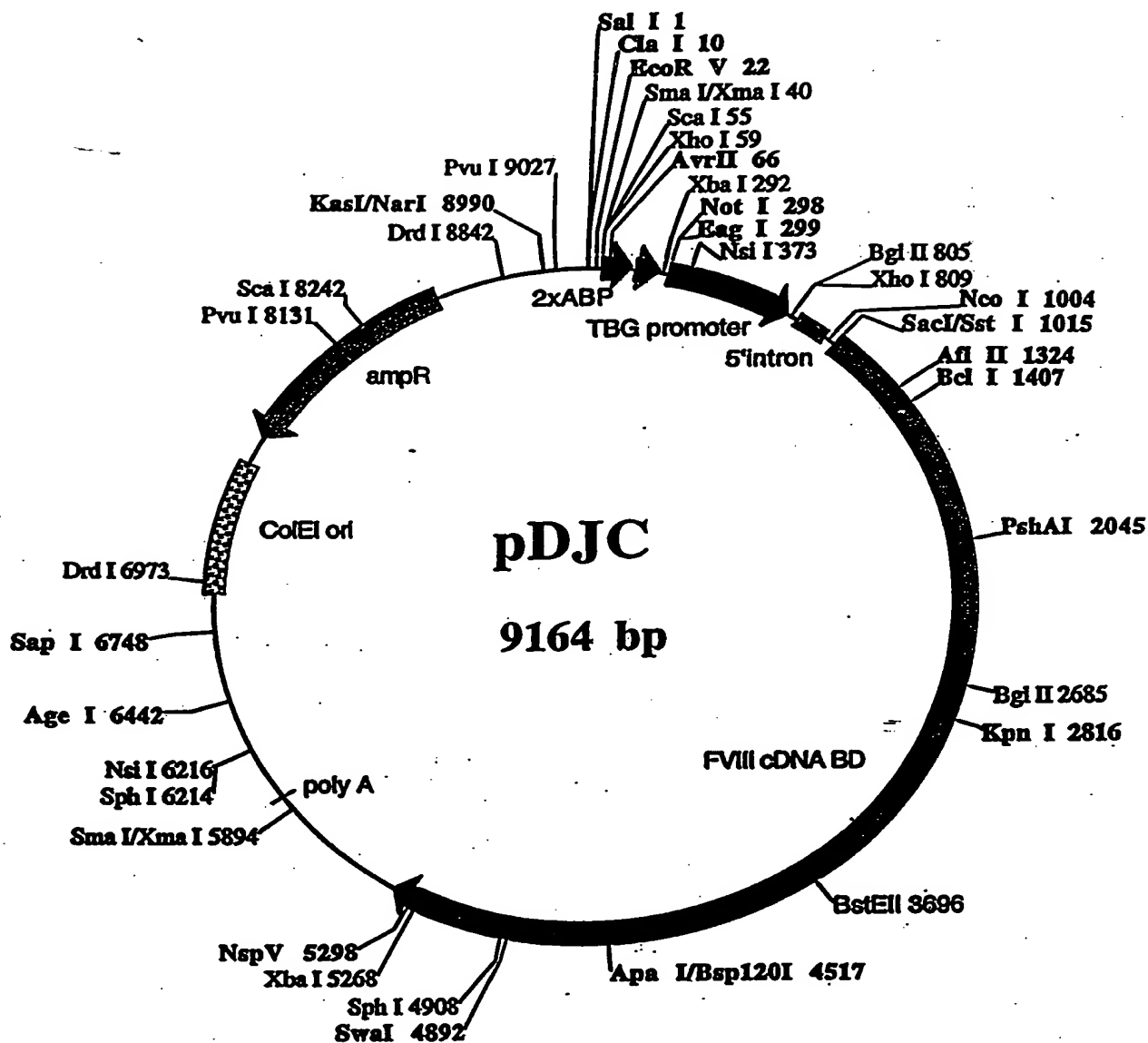
	4225	4230	4235	4240	4245	4250	4255	4260	4265	4270						
	*	*	*	*	*	*	*	*	*	*						
pDJCcoding	CAG	GGA	AAT	CAA	GAC	TCC	TTC	ACA	OCT	GTC	GTG	AAC	TCT	CTA	GAC	CCA
1. p25Dcod	4230				4240			4250			4260				4270	
[16902]	CAG	GGA	AAT	CAA	GAC	TCC	TTC	ACA	OCT	GTg	GTG	AAC	TCT	CTA	GAC	CCA>
	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^
pDJCcoding	CAG	GGA	AAT	CAA	GAC	TCC	TTC	ACA	OCT	GTC	GTG	AAC	TCT	CTA	GAC	CCA

	4275	4280	4285	4290	4295	4300	4305	4310	4315	4320
	*	*	*	*	*	*	*	*	*	*
pDJCoding	CCG	TTA CTC	ACT CGC	TAC CTT	CGA ATT	CAC CCC	CAG AGT	TGG GTG	CAC	
1. p25Dcod		4280		4290		4300		4310		4320
[16902]	CCG	TTA CTC	ACT CGC	TAC CTT	CGA ATT	CAC CCC	CAG AGT	TGG GTG	CAC	
	^^	^^	^^	^^	^^	^^	^^	^^	^^	^^
pDJCoding	CCG	TTA CTC	ACT CGC	TAC CTT	CGA ATT	CAC CCC	CAG AGT	TGG GTG	CAC	

		4325	4330	4335	4340	4345	4350	4355	4360	4365	
		*	*	*	*	*	*	*	*	*	
pDJCoding		CAG ATT GCC CTG AGG ATG GAG GTT CTG GGC TGC GAG GCA CAG GAC CTC									
1. p25Dcod		4330		4340		4350		4360			
[16902]		CAG ATT GCC CTG AGG ATG GAG GTT CTG GGC TGC GAG GCA CAG GAC CTC>									
		^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^	^^^
pDJCoding		CAG ATT GCC CTG AGG ATG GAG GTT CTG GGC TGC GAG GCA CAG GAC CTC									

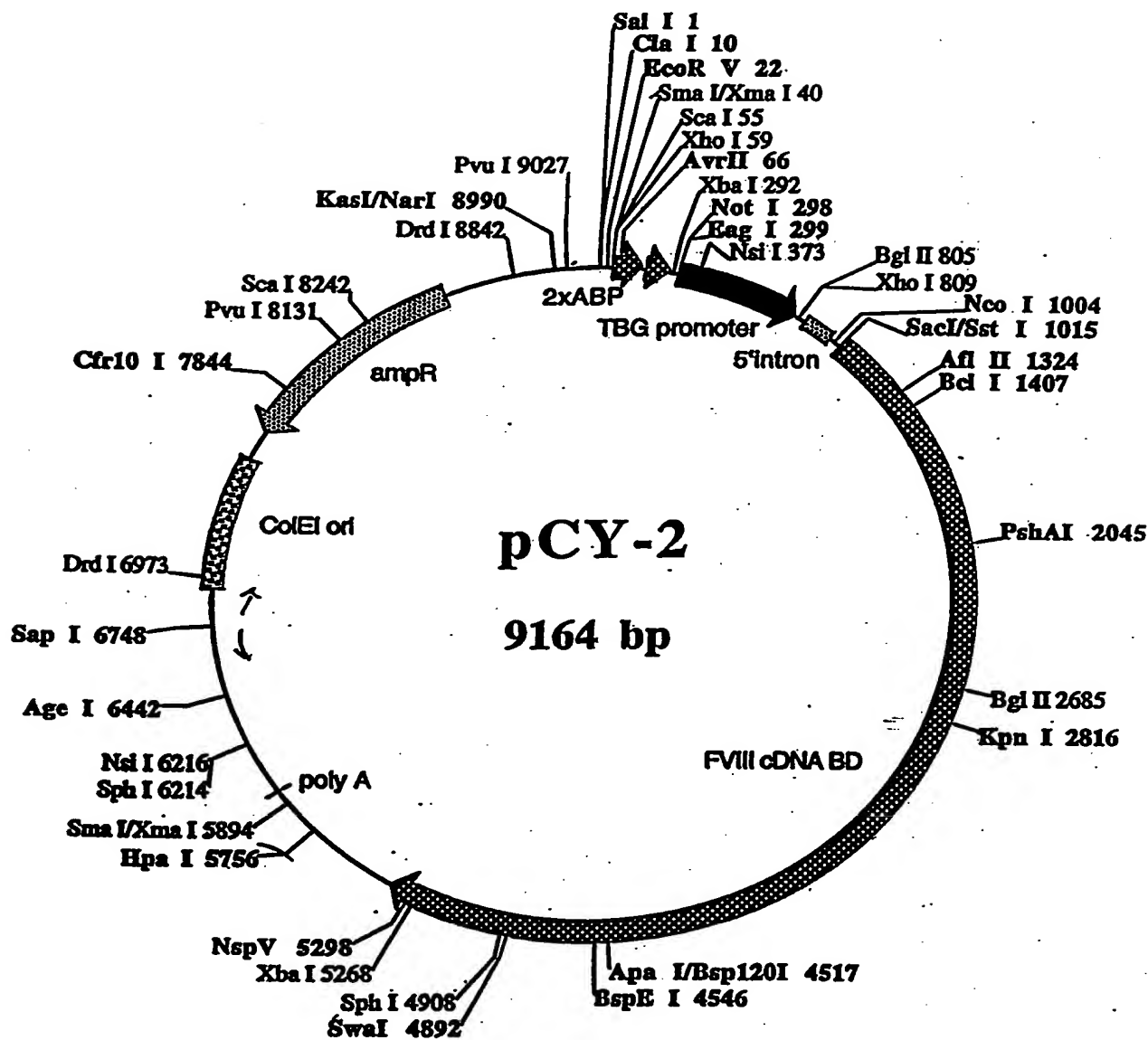
4370
 *
 pDJCcoding TAC TGA
 |
 1. p25Dc4370
 (16902) TAC TGA→
 ^^^ ^^^
 pDJCcoding TAC TGA

FIG. 6



000210-09229560

FIG. 7



00000-09225560

FIG. 8

Human Factor VIII cDNA Synthetic Approach

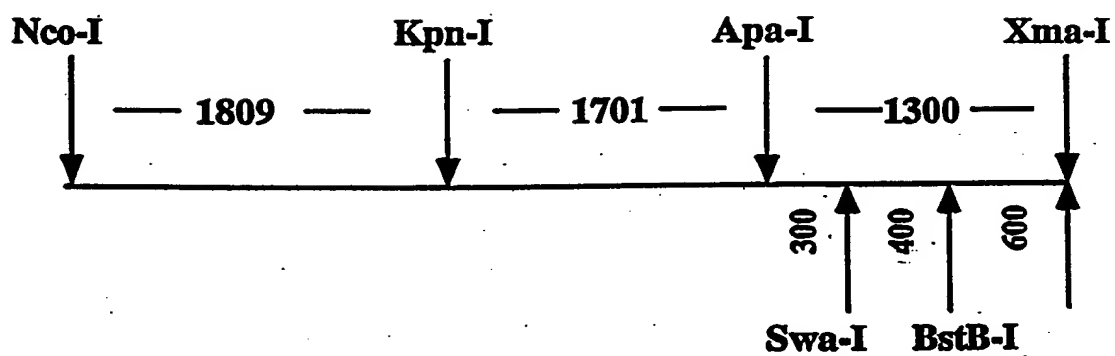
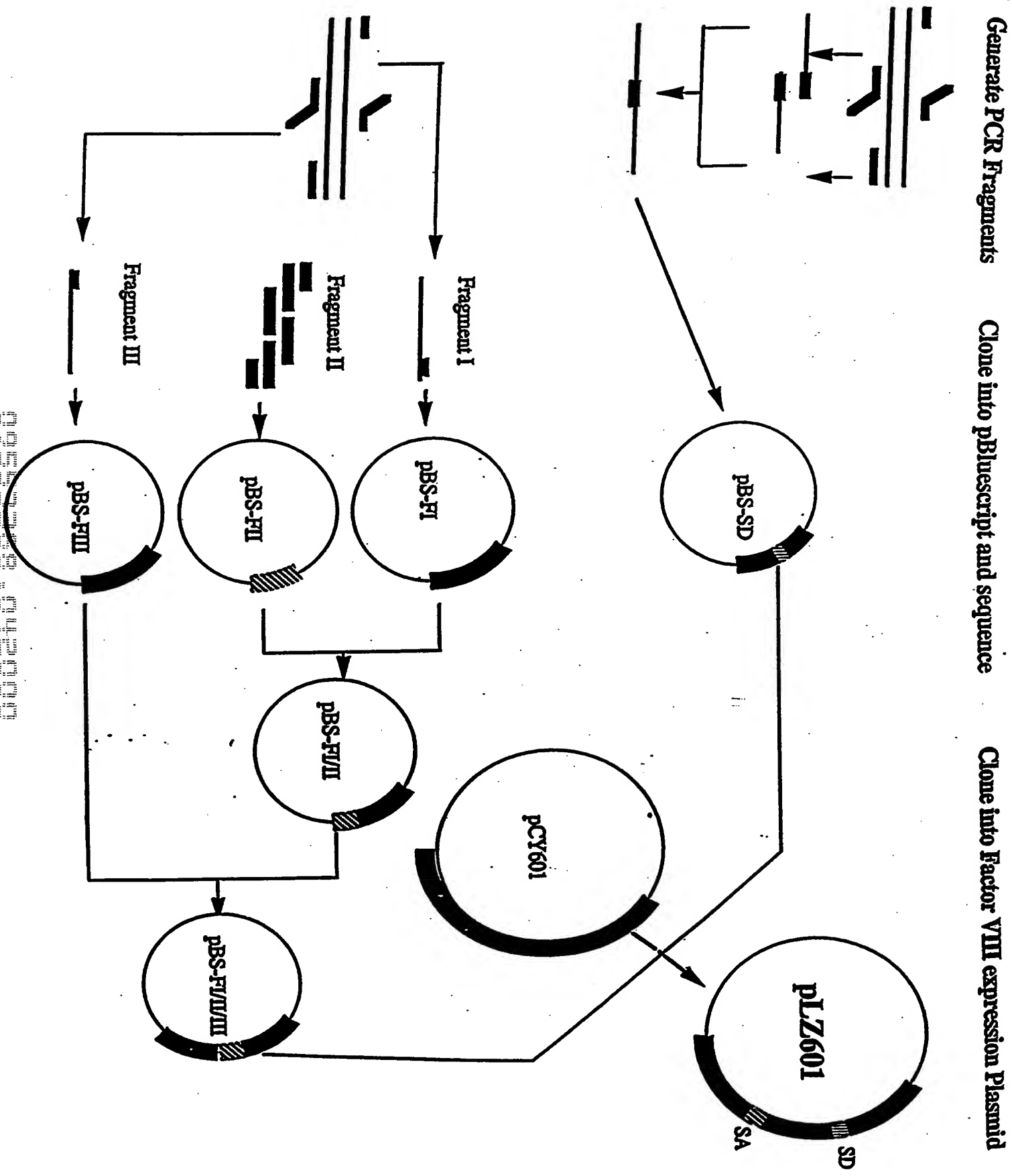


FIG. 9



09550000 042000

FIG. 10

Full-length Factor VIII cDNA

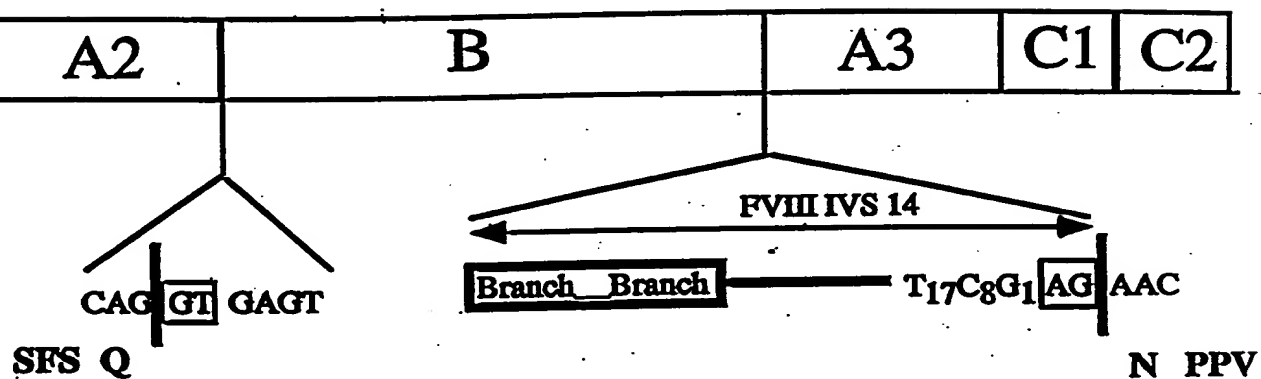


FIG. 11

**Factor VIII Full Length cDNA
(Exon-Intron Boundary)**

00000 0922560

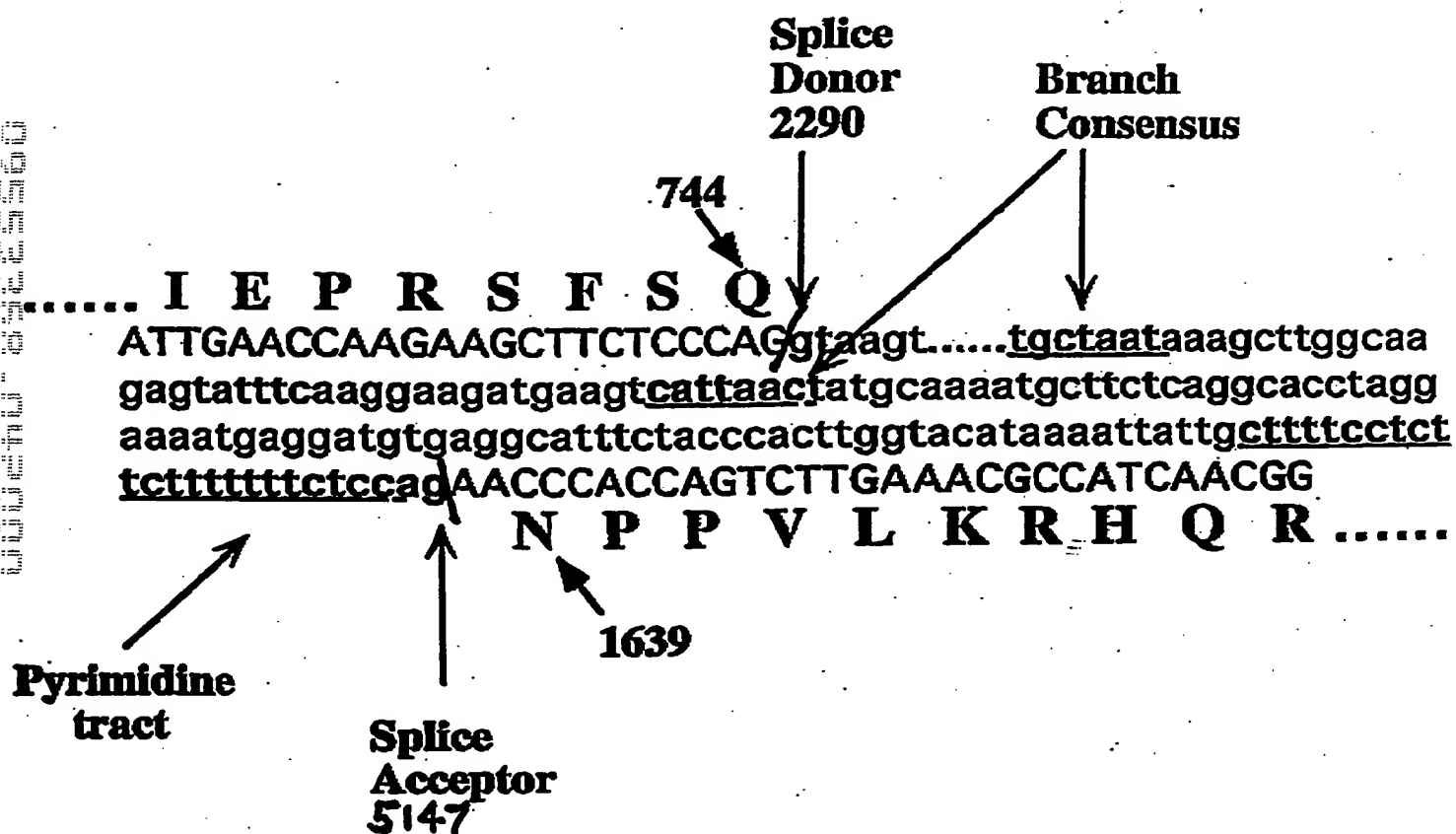


FIG. 12

Human Factor VIII cDNA: Intron Engineering Considerations

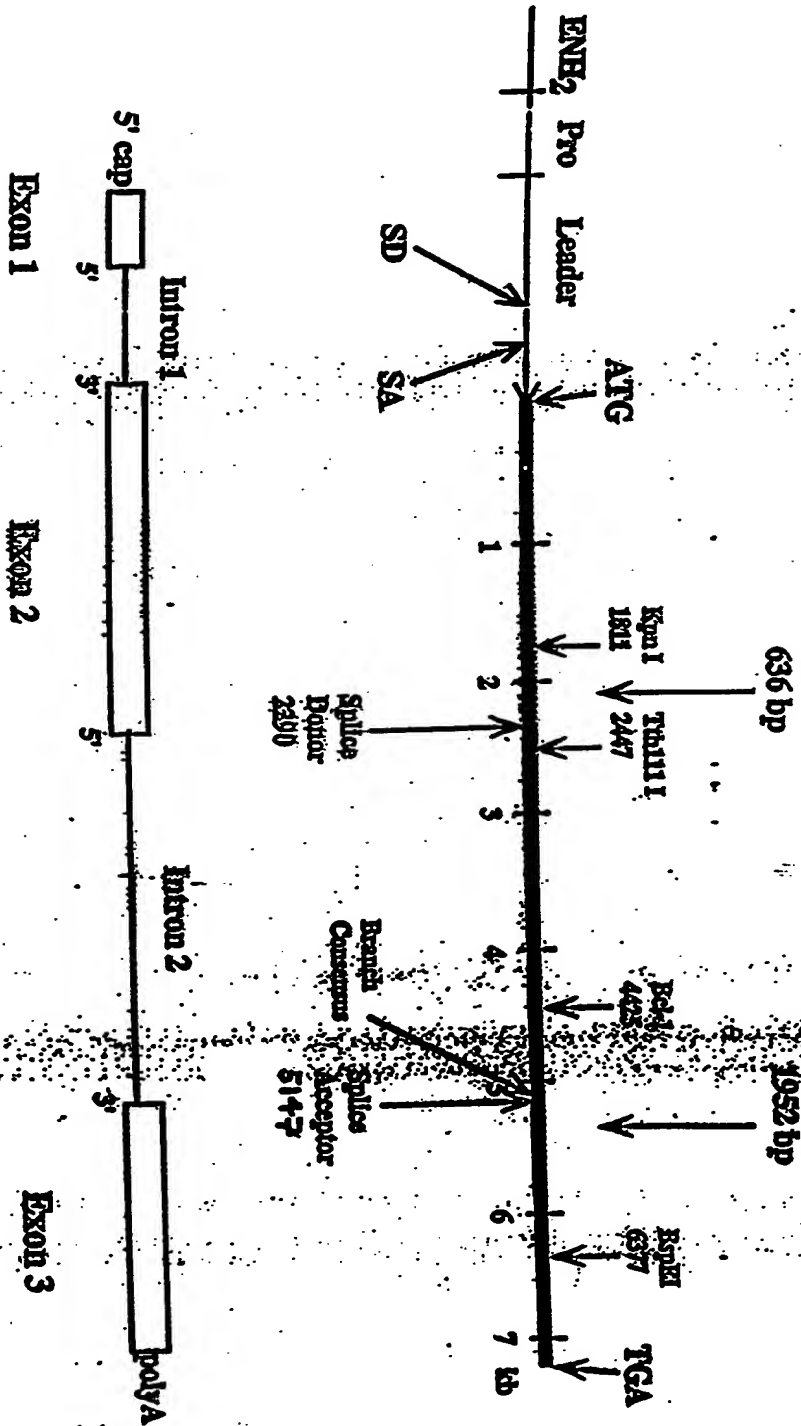


FIG. 13

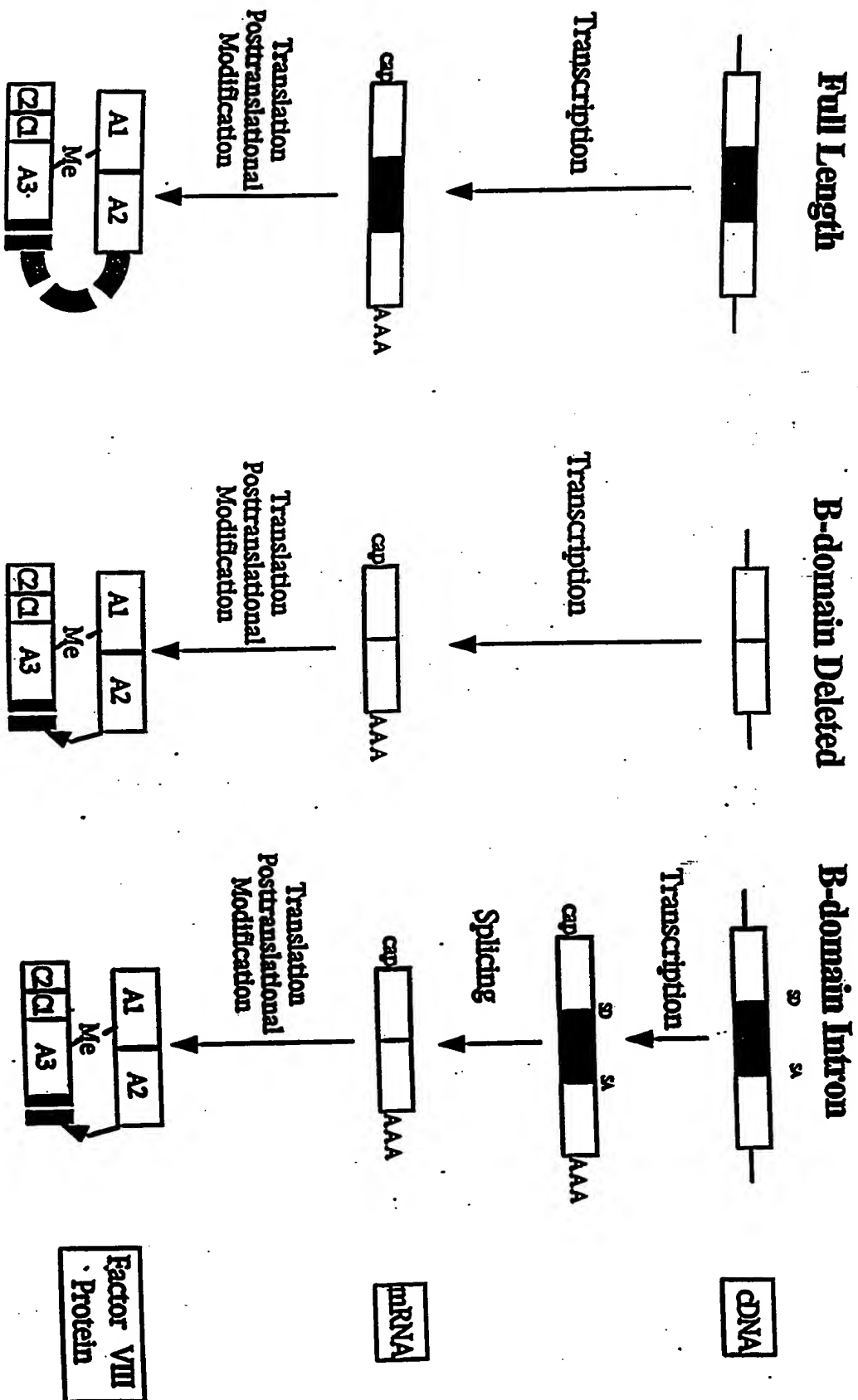


FIG. 14

**Relative Expression Levels of
Factor VIII Plasmids**

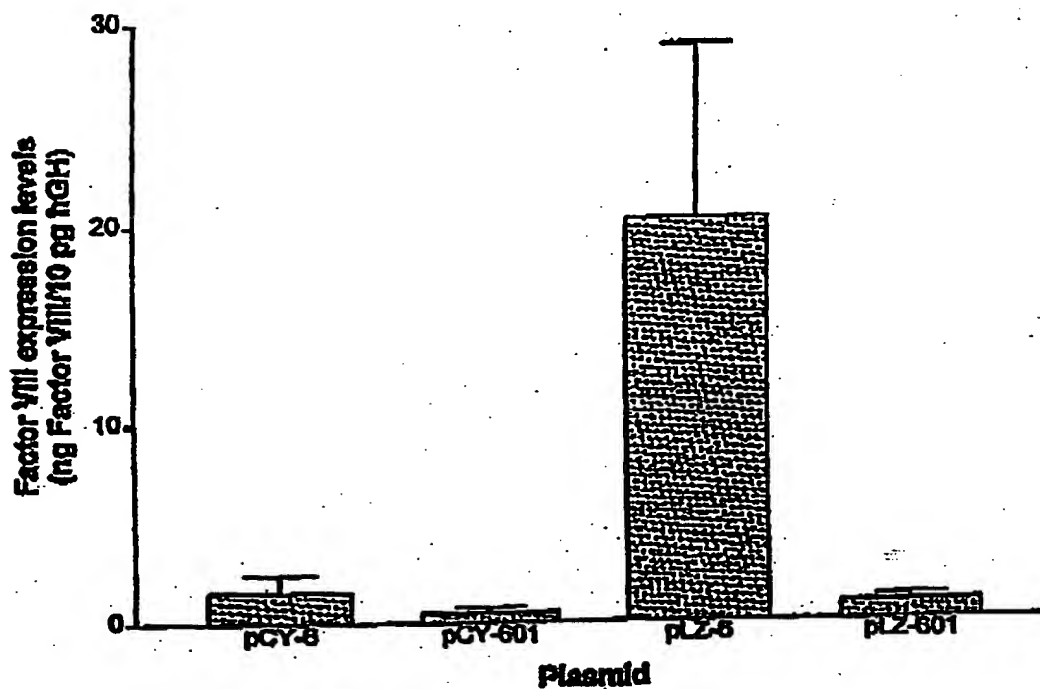


FIG. 15

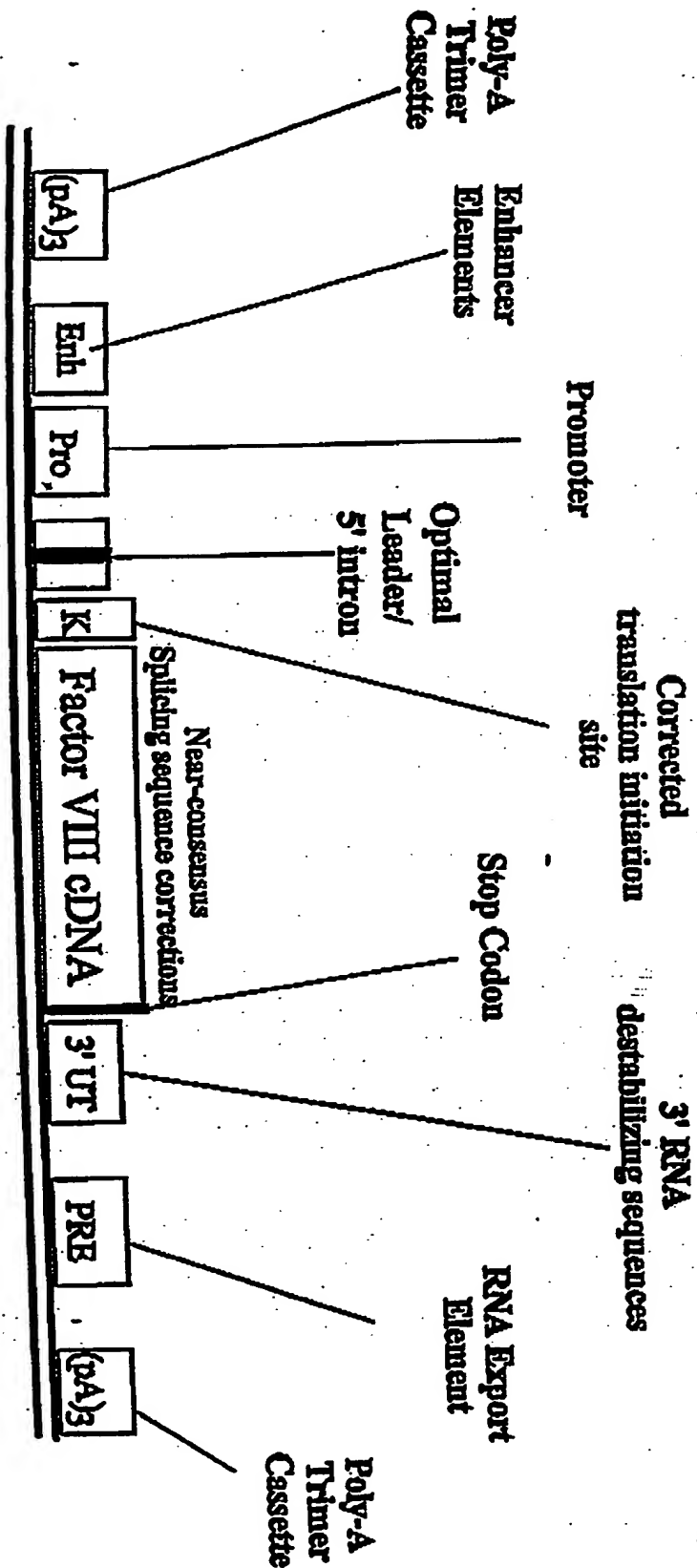


FIG. 16

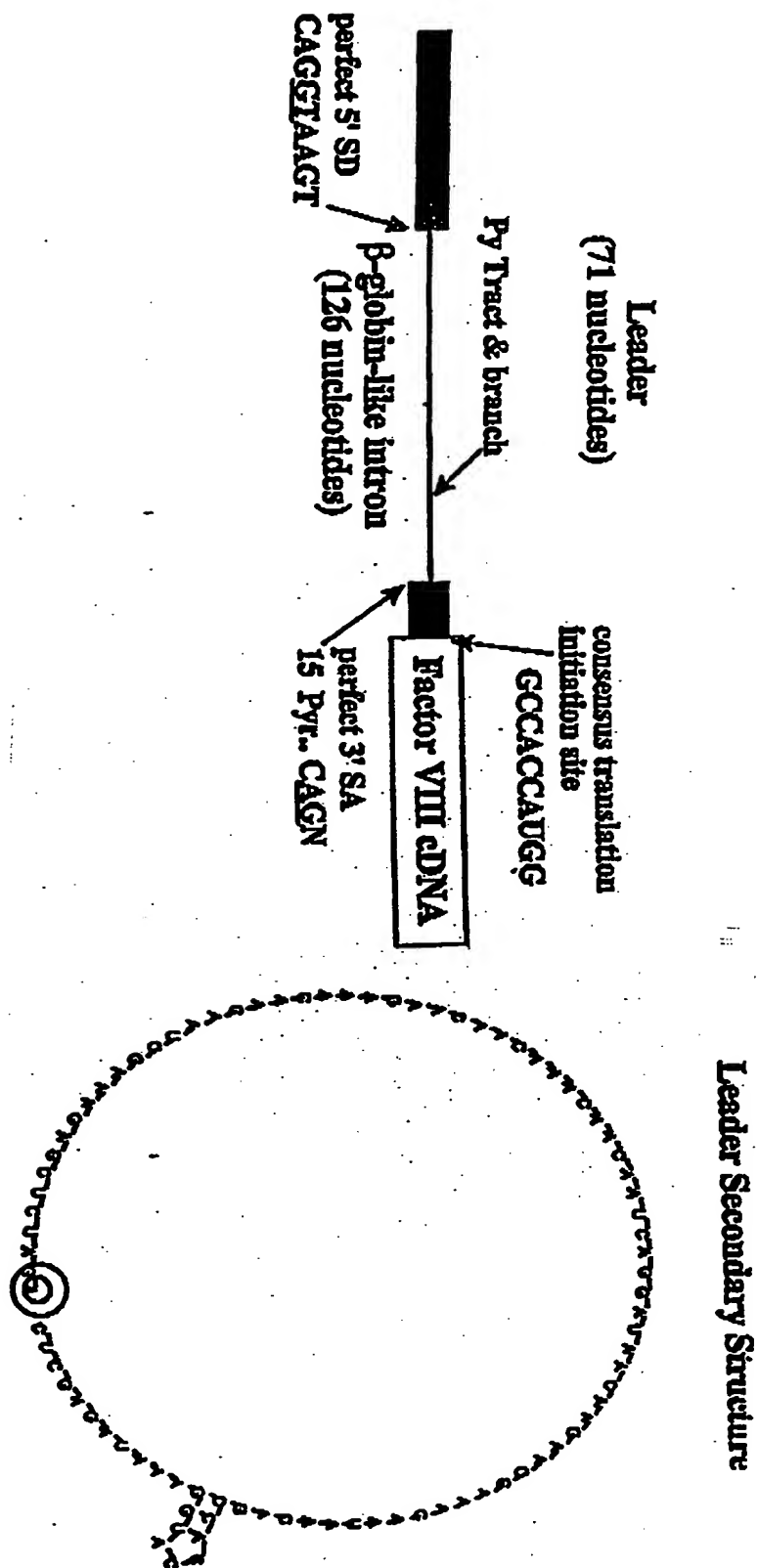


FIG. 17

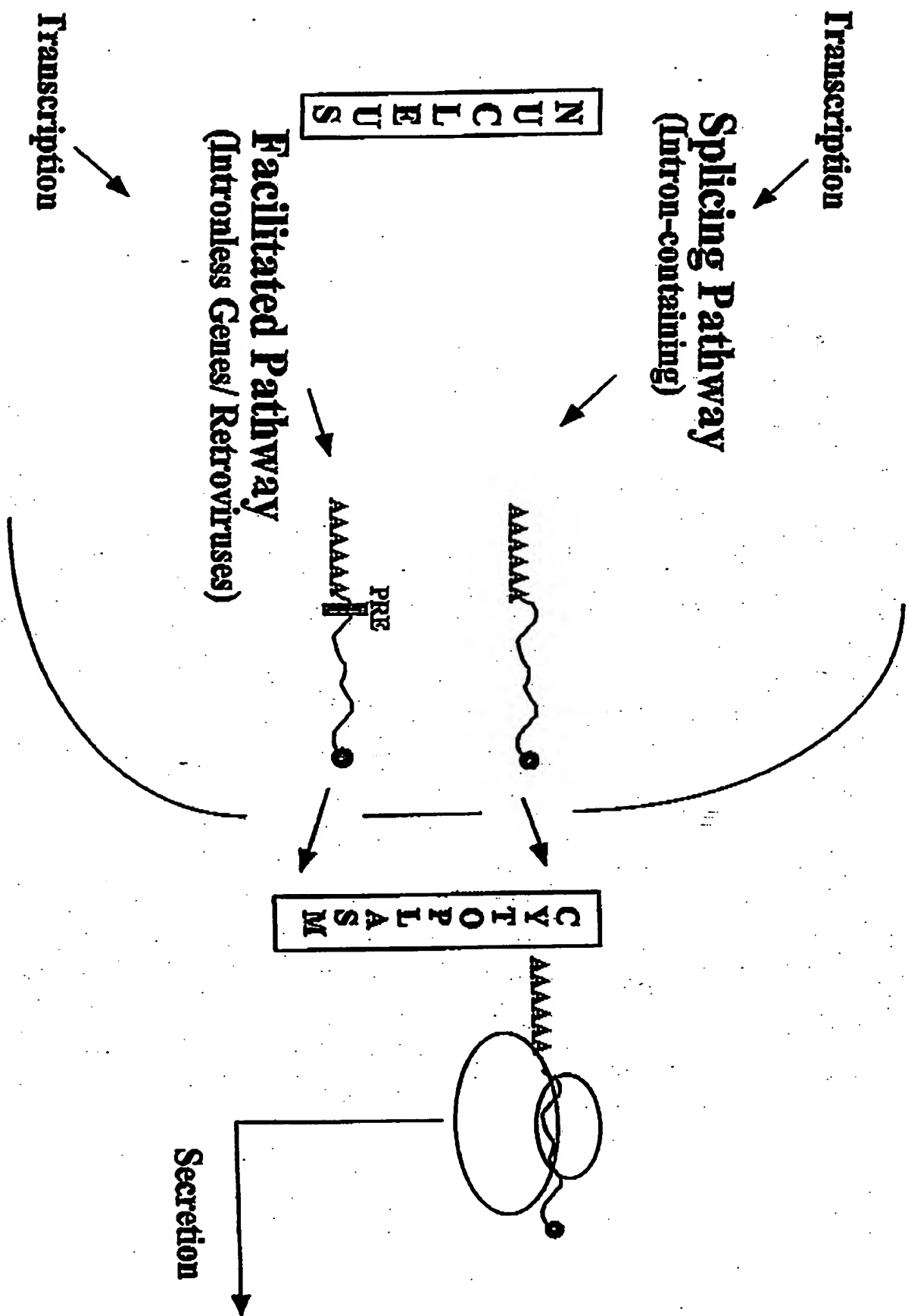
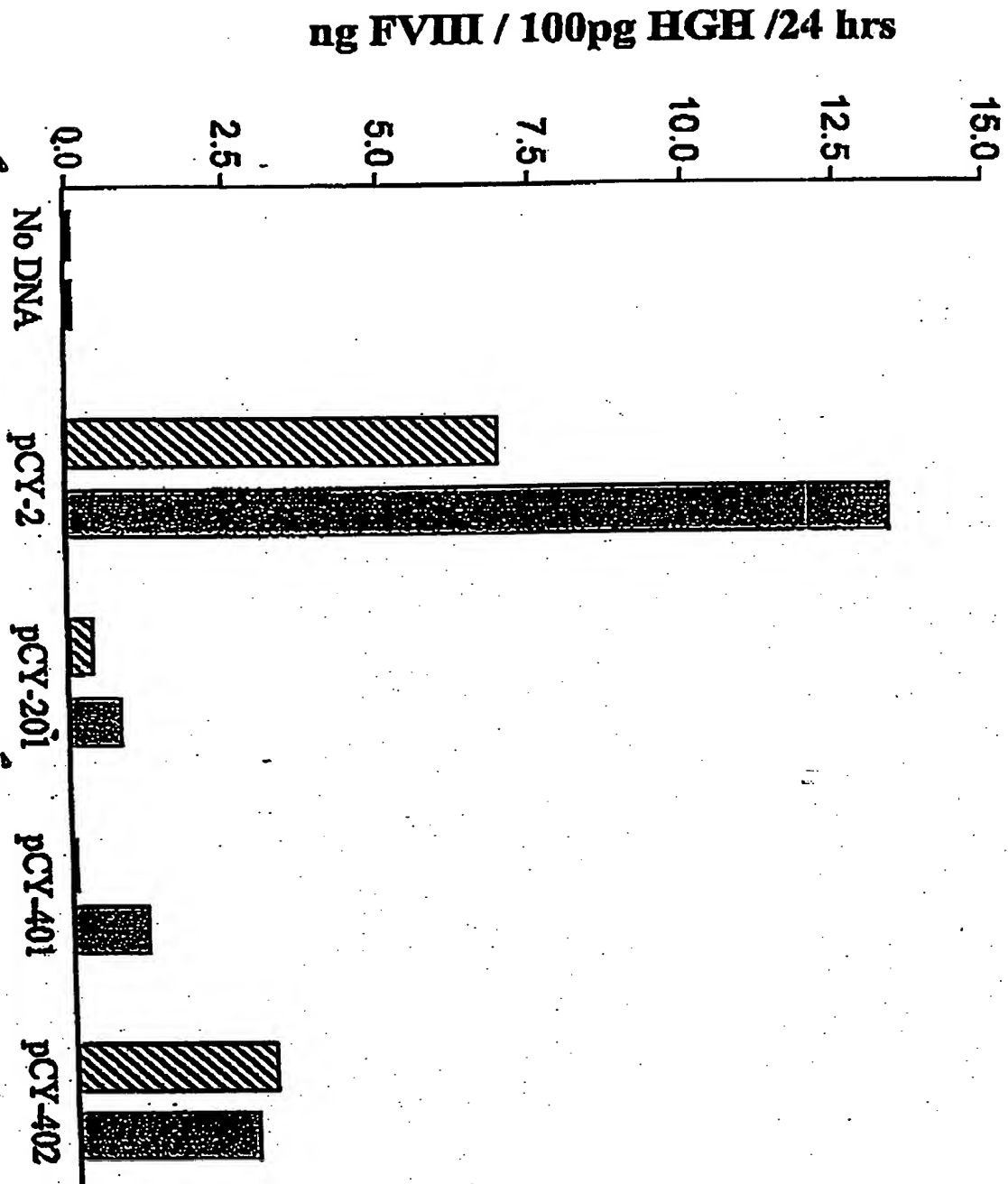


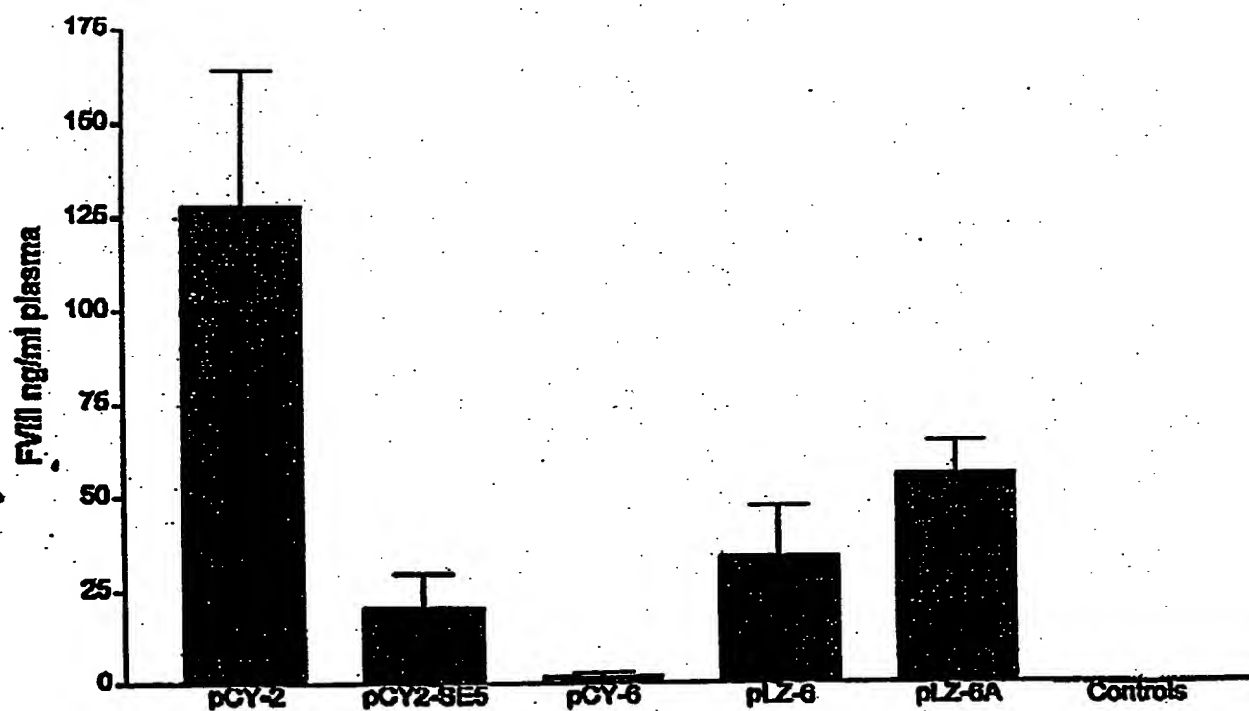
FIG. 18



0053369 042000

FIG. 19

**#889 *in vivo* test
of Factor VIII expression plasmids
Modified Coatest
12-10-97**



A Potent Tissue-specific Enhancer Made of Clustered Liver-specific Elements from the Human Alpha-1 Microglobulin/Bikunin Gene*

FIG. 20

5' AGCTTAATTTTAAAGCA CTCAAAGTC CAAGTGGCCCTGCGAGCAT
HNF-1 HNF-4
TTACTCTCTC TGTTTGCTCT GGTTAATAAT CTCAGGAGC A CAACATTC
HNF-3 HNF-1 HNF-3 3'

From : P. Rouet...J.P. Salier, (1992) J. Biol. Chem 267 No.29, pp. 20765-20773

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0953368 042000

A 218-bp Fragment of the Human Thyroxin-Binding Globulin (TBG) Gene Contains Full Promoter Activity

FIG. 21

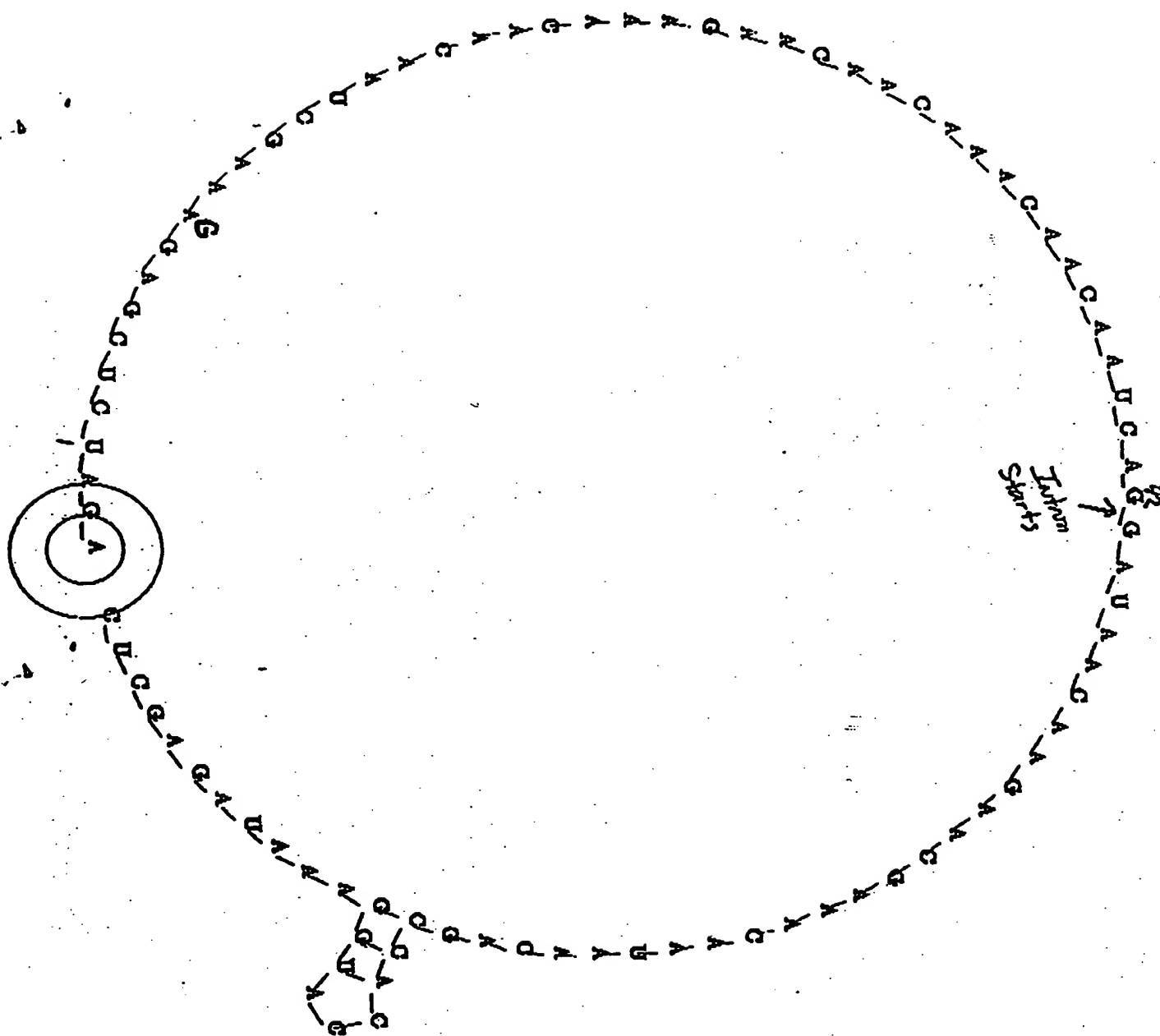
CTTCTCT TTTCTTTTAC ATGAA GGGTCTGGCAGCCAA GCAAT CACT CAAAGTTCAA
CCTATCAT TTTGGCTTGT TCCTCTGG CCTGGTTTG TACATCAG CTTGAAAT
ACCATCCAG GGTAAATGCT GGG GTTAATTATAAC TAAGAGTGTCTAG TTT GCAAT
ACAGGACATGC TATAA AAATGGAAGATGTTGCTTCTGAGAGATA
5 3'

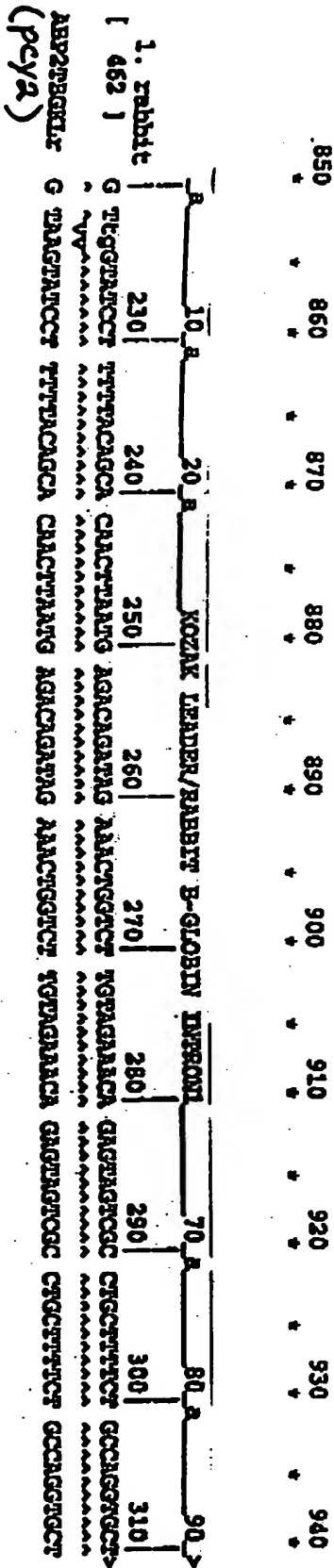
From : Y. Hayashi.....S. Refetoff. (1993), Molec. Endo. 7 No. 8, pp. 1049-1060

The Immune Response Corporation

0053358.042000

FIG. 22

[illegible]



1. rabbit
[462]
GACTCTCTC CCGTGGCTG TTTGATTTT CTGAG
GACTCTCTC CCGTCTCTT TTTCTCTTT CTGAG

Endothelium-Specific Promoters and Enhancers



FIG. 24

Promoter Name	Characteristics	Reference
1) Endothelin-1	204 bp; has enhancer seq, TATAA box, TS mapped	Lee et. al. <i>JBC</i> 265 No. 18, 1990. ←
2) Flt-1 (fms-like tyrosine kinase)	~1 kb, no enhancer, TATAA box, TS mapped	Morishita et. al. <i>JBC</i> 270 No. 46, 1995
3) Nitric Oxide Synthase	~1 kb, GATAA box, TS mapped	Zhang et. al. <i>JBC</i> 270 No 25, 1995
Enhancers		
1) c-Fos SRE	60 nt's, non-tissue specific, active in resting or dividing cells	Treisman, <i>Cell</i> 46, 1986 ←
2) hTF/mTie-2	Hybrid design, 72 nt's, all endo's	1998

FIG. 25

Human Factor VIII In Vivo Expression Viral vs Tissue-Specific Promoter

